REMARKS

Claims 1-8 and 11-13 were pending in the instant application as of the issuance of the Office Action dated November 24, 2006. Claims 6, 7 and 13 were previously withdrawn as being directed to a non-elected invention. By the current amendments, claim 1 has been amended to merely to reword the language of the claim. Support for the amendment can be found throughout the specification and in the claims as originally filed. No new matter has been added.

Following entry of the foregoing amendments, claims 1-8 and 11-13 will remain pending. Applicants further note that the foregoing amendments have been made solely in order to expedite examination and in no way should be construed as acquiescence to the validity of the rejections set forth in the Office Action.

Election/ Restrictions

Applicants acknowledge the election of Group III, *i.e.*, claims 1-5, 8 and 11-12 (drawn to a method of inhibiting an activity of a G1 cdk comprising the use of a "substance that includes a peptide," and wherein a carrier molecule is neither suggested nor required) in response to the restriction requirement under 35 U.S.C. § 121 as set forth in the Office Actions of January 6, 2006 and May 10, 2006.

Applicants further note that in the response dated September 11, 2006, Applicants *traversed* the restriction requirement at least with respect to Groups III and IV, asserting that "a finding of novelty of the use of the peptide fragment necessitates a finding of novelty of claims directed to the use of peptide fragments linked to the specified coupling partners." Applicants submit that although claims 6, 7 and 13 have been withdrawn from examination, Applicants' traversal was not specifically addressed in the present Office Action. Accordingly, Applicants respectfully request reconsideration and withdrawal of the restriction requirement with respect to Groups III and IV.

In addition, Applicants acknowledge the election of the following species ***for search purposes only***: cdk4 as the G1 cdk; a single pure compound as the "substance"; Rb phosphorylation as the specific G1 cdk "activity" to be inhibited; the elected substance is identical to the peptide of 40 amino acids (or less) that is described in claim 1; and residues 16-35 of $p21^{WAF}$ as a specific substance that falls within the scope of claim 1.

In this regard, it is Applicants' understanding that upon the allowance of a generic claim, Applicants will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 C.F.R. §1.141 *et seq.* Accordingly, upon allowance of the elected species, Applicants request that the search be extended to the remaining species. Applicants' election of the foregoing species is without prejudice to Applicants' rights to pursue non-elected subject matter in this and other applications.

Priority Documents

Applicants submit that certified copies of each of the foreign priority documents were forwarded to the U.S. Patent Office from the International Bureau during pendency of corresponding International Application No. PCT/GB97/01250 and are publicly available on PAIR in the file history of U.S. Application No. 09/180269 of which the present application is a continuation. Accordingly, as provided in M.P.E.P. § 201.14(b)(II), the filing of certified copies of the priority documents in the present application is unnecessary. However, for the Examiner's convenience, copies of the priority applications are submitted herewith.

Information Disclosure Statement

At page 10, the Office Action indicates that certain references cited in an Information Disclosure Statement filed on March 16, 2004 "were stricken... because they have not been received, and are not present in the parent file." Although submission of those references previously forwarded in a parent application is unnecessary in accordance with 37 CFR §1.98(d), Applicants submit herewith a Supplemental Information Disclosure Statement, PTO Form SB/08 and a copy of those references not previously considered. Accordingly, Applicants respectfully request that the Examiner consider the enclosed references and acknowledge such consideration by initialing and returning a copy of the enclosed PTO Form SB/08.

Rejection of Claims 1-5, 8, 11 and 12 Under 35 U.S.C. § 112, Second Paragraph

Claims 1-5, 8, 11 and 12 have been rejected as "failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention" on the ground that

> [t]he issue here concerns the relationship between the phrase 'peptide fragment' and the phrase 'the peptide fragment... coupled to a non-peptidyl coupling partner...'. At first blush, the term 'wherein' would seem to be implied, i.e., the following: A method of inhibiting... comprising contacting... with a substance which is a peptide fragment..., **wherein** the peptide fragment is coupled to a non-peptidyl coupling partner [...] However, this appears not to be intended. (Office Action, pages 2-3)

Applicants respectfully disagree. Applicants submit that the plain language of the claim renders the scope of the claimed invention sufficiently definite in accordance with 35 U.S.C. § 112, second paragraph. However, solely in the interest of expediting prosecution and in no way acquiescing to the validity of the rejection, Applicants have amended claim 1, substantially as suggested by the Examiner. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

Rejection of Claims 1-3 Under 35 U.S.C. § 102(a)

Claims 1-3 have been rejected as being anticipated by Ball *et al.* (*Current Biology* (1996) 7:71-80) (hereinafter referred to as "Ball") on the ground that "Ball discloses the invention substantially as claimed."

Applicants respectfully disagree. The present application claims priority to each of UK Application No. 9609521.1, filed on May 7, 1996, and to UK Application No. 9621314.5, filed on October 9, 1996. Applicants submit that these priority applications incorporate the teachings, including all of the data, described by Ball (*e.g.*, figures 1-5 in Ball correspond to Figures 1-4, 8, 9 and 11 in the priority applications) and predate the December 20, 1996 publication date of this reference. Accordingly, Ball does not qualify as prior art against the present application and withdrawal of this rejection is respectfully submitted.

Rejection of Claims 1-3 Under 35 U.S.C. § 103(a)

Claims 1-3 have been rejected as being unpatentable over Nakanishi *et al.* (*EMBO Journal* (1995) 14(3):555-563) on the ground that

> Nakanishi discloses... that peptides containing the following sequence inhibit cyclin-dependent kinases: WMNFDFXXXXPLEGXXXWXXV. The issue here is that instant claim 1 does not actually require that the peptide in question contain the subsequence RRyFz... Thus, when one is using a fragment of p21, it may be true that the subsequence RRyFz must be present, but when one is using '**derivative** of a fragment', it is only the fragment that must contain the subsequence RRyFz, and not the derivative of the fragment. (Office Action, pages 5-6)

Applicants respectfully disagree. However, solely in the interest of expediting examination and in no way acquiescing to the validity of the rejection, Applicants have amended claim 1 to explicitly require that both the peptide fragment and its derivative comprise at least the motif xxRRyFz. Accordingly, Applicants respectfully request reconsideration and withdrawal of the foregoing rejection.

Rejection of Claims 1-3 Under 35 U.S.C. § 103(a)

Claims 1-3 have been rejected as being unpatentable over Chen *et al.* (*J. Molecular & Cellular Biology* (1996) 16(9):4673-4682) (hereinafter referred to as "Chen") on the ground that "Chen discloses... the following peptide: ACRRLFGPVDSE. Chen also discloses that this, and other peptides inhibit cyclin dependent kinases."

Applicants respectfully traverse this rejection. Applicants note that the present application claims priority to UK Application No. 9609521.1. This application, which predates the September 1996 publication date of Chen, discloses that N-terminal peptides of p21 as well as fragments and derivatives thereof inhibit cdk activity. Accordingly, Applicants submit that the Chen reference does not qualify as prior art to the present application and withdrawal of this rejection is respectfully requested.

Rejection of Claims 1-3 Under 35 U.S.C. § 103(a)

Claims 1-3 have been rejected as being unpatentable over Xiong *et al.* (*Nature* (1993) 366(6456):701-704) (hereinafter referred to as "Xiong") or Harper *et al.* (*Molecular Biology of the Cell* (1995) 6:387-400) (hereinafter referred to as "Harper") in view of Xiong on the ground that

> Xiong and Harper both teach that p21 inhibits cyclin dependent kinases; Xiong provides the sequence of p21. Certainly, the teachings of Harper and Xiong taken together disclose a method of inhibiting the activity of a G1 cdk by contacting the cdk with a

> peptide that comprises (a) a fragment of less than 40 amino acids of p21 and (b) a 'carrier' peptide, which happens to be another portion of p21. This conclusion is also reached by considering Xiong by itself. As it happens, however, this particular embodiment is excluded by the claims. But what is not excluded is 'non-p21 peptide sequences' that are rendered obvious by Xiong. (Office Action, page 7).

Applicants respectfully disagree. Neither Xiong alone or in combination with Harper teach or suggest the presently claimed invention which is directed to a method of inhibiting the activity of a G1 Cdk by contacting the ckd with ***a peptide fragment of 40 amino acids or less of p21*** or a derivative thereof, wherein the fragment or derivative is optionally coupled to a non-peptidyl coupling partner or, alternatively, a non-p21 peptide sequence and wherein the peptide fragment or derivative comprises at least the motif xxRRyFz.

Specifically, while Xiong teaches the full-length sequence of p21, this reference does not teach or suggest that fragments of p21 of 40 amino acids or less would be capable of inhibiting the activity of a G1 Cdk. Nor does Xiong provide any guidance whatsoever regarding which portions of p21 are involved in regulating Cdk activity. Accordingly, even if one were skilled in the art were to seek out biologically active p21 fragments, the skilled artisan would be compelled to design and test a vast number of possible fragments with little expectation of success.

Moreover, Harper not only fails to cure the deficiencies of Xiong, but actually teaches away from the presently claimed invention. Indeed, while Harper does teach that full-length p21 inhibits G1 Cdks, Harper teaches that amino terminal residues 1-60 of p21 ***"lacked appreciable inhibitory activity"*** (page 391, last paragraph of column 1). Thus, the skilled artisan presented with the combined teachings of these references would not have been motivated to make p21 fragments of 40 amino acids or less which contain the xxRRyFz motif with any expectation that such fragments would inhibit G1 Cdk activity.

Further, Xiong alone or in combination with Harper fails to teach or suggest fragments of p21 coupled to non-p21 peptide sequences, let alone that such substances would be expected to have activity. Xiong merely teaches the full-length p21 which would not be considered by the skilled artisan to be a small peptide of p21 ***coupled*** to a non-p21 peptide sequence whether or not the p21 sequence was modified as suggested in the Office Action. The specification clearly indicates that ***"a non-p21 peptide sequence" refers to a heterologous or foreign coupling partner*** (see page 14, lines 10-11 of the specification). Moreover, the term "coupled" in the

claimed method indicates that the p21 peptide fragment has been manipulated in some way so as to attach another non-p21 peptide sequence.

In view of the above, Applicants submit that neither Xiong nor Harper, alone or in combination, render the claimed invention obvious, and withdrawal of this rejection is respectfully requested.

Rejection of Claim 1 Under 35 U.S.C. § 103(a)

Claim 1 has also been rejected as being unpatentable over Lin *et al.* (*Molecular and Cellular Biology* (1996) 16(4):1786-1793) (hereinafter referred to as "Lin") on the ground that "Lin discloses inhibition of cdk's by p21; also disclosed, however, is inhibition of cdk's by peptides which are mutants of p21. As such the limitation of a 'non-p21 sequence' is met by the reference."

Applicants respectfully disagree. Lin teaches a number of full-length p21 mutants which either failed to bind or had reduced binding to cyclin E (see page 1788). As discussed above, full-length p21 would not be considered by the skilled artisan to be a small peptide of p21 ***coupled*** to a non-p21 peptide sequence whether or not the p21 sequence was modified, *i.e.*, mutated. Thus, the p21 mutants of p21 taught by Lin would not render the presently claimed invention obvious and withdrawal of this rejection is respectfully requested.

Rejection of Claims 1 and 5 Under 35 U.S.C. § 103(a)

Claims 1 and 5 have been rejected as being unpatentable over Toyoshima *et al.* (*Cell* (1994) 78:67-74) (hereinafter referred to as "Toyoshima") on the ground that

> Toyoshima discloses the inhibition of cdk's by p27. The issue here is that the term 'fragment' in instant claim 1 could mean just one single amino acid; thus, any amino acid that is present in p21 would qualify. As such, nearly any peptide that inhibits a G1 cdk would be encompassed by the claims. But even if applicants were to amend claim 1 to require that the 'substance' in question contain a tetrapeptide subsequence of p21, the requirements of such a claim would be met by Toyoshima. For example, the peptide disclosed on page 68 (figure 1) of Toyoshima contains the pentapeptide LFGPV; this pentapeptide is also contained within p21. Similarly, the Toyoshima peptide contains the subsequence PLEG which is also contained within p21. This ground of rejection is directed at the subgenus of claim 1 which is drawn to a fragment of 40 amino acids or less of p21 that is coupled to a non-p21 peptide sequence.

Applicants respectfully disagree. Applicants submit that the plain language of claim 1 clearly requires that the p21 fragment or derivative comprises at least the motif xxRRyFz. Accordingly, the peptides disclosed by Toyoshima do not teach or suggest each and every element of the claimed invention, *i.e.*, the motif xxRRyFz. Accordingly, Applicants respectfully request reconsideration and withdrawal of the foregoing rejection.

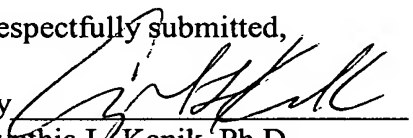
SUMMARY

Applicants respectfully submit that the above-identified application is in condition for allowance. If a telephone conversation with Applicants' attorney would expedite prosecution of the above-identified application, the Examiner is urged to call Applicants' Attorney at (617) 227-7400.

The Commissioner is hereby authorized to charge any deficiency, or credit any overpayment, in the present filing to Deposit Account No. 12-0080 under Order No. CCI-007USDV, from which the undersigned is authorized to withdraw.

Dated: April 24, 2007

Respectfully submitted,

By 

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